Written Testimony
Committee on Government Reform
United States House of Representative
Hearing on Reduced Exposure/Reduced Risk Tobacco Products:
An Examination of Potential Public Health Impact
and Regulatory Challenges
June 3, 2003

Dorothy K. Hatsukami, Ph.D.
Professor of Psychiatry
University of Minnesota Medical School

As an invited participant to the Committee on Government Reform hearing entitled, ***Reduced Exposure/Reduced Risk Tobacco Products: An Examination of the Potential Public Health Impact and Regulatory Challenges***, I have been asked to address the following four questions.

In your opinion, do reduced exposure/reduced risk products represent an acceptable alternative for current smokers who have been unable to quit smoking?

The best scientifically known intervention to reduce harm among smokers is cessation. Whether reduced exposure/reduced risk products represent an acceptable alternative for current smokers who are unable to quit is dependent on whether or not we have been able to develop and provide the best cessation methods to treat smokers. *Therefore, greater resources and time should be devoted to research that increases our understanding of factors associated with tobacco addiction. This understanding, in turn, will inform us of how to develop more effective treatments for smokers who are unable to quit.*

If smokers continue to be unable to quit given the best interventions, whether or not reduced exposure/reduced risk products represent an acceptable alternative depends also on scientific knowledge. The science needs to show that the extent of reduction that is achieved with these products is associated with a significant reduction in disease risk and that the impact of these products at the population level is not negative. Furthermore, it is imperative that these areas of investigation be conducted by organizations that are independent of the producers and marketers of these products.

To determine if reduced risk products are suitable alternatives, several aspects contributing to harm reduction must be examined. For harm reduction to occur, there must be a significant reduction in morbidity and mortality even with the continued use of tobacco products or constituents of tobacco products. However, in order to demonstrate harm reduction, several years of investigation must be conducted with that particular product. Because this type of study is not likely to be feasible, other methods for assessing the impact of these products on public health must be considered. In the Institute of Medicine report, *Clearing the Smoke, Assessing the Science Base for Tobacco Harm Reduction*, a model was described that would help to assess total harm associated

with reduced exposure/reduced risk products. First, the *toxicity of the product itself* should be determined. Toxicity should be measured in the tobacco product itself and in the case of cigarettes, when the tobacco product is heated or combusted. Furthermore, toxins resulting from combined use of tobacco products should also be examined based on observations of how individuals actually combine the use of these products.

Second, the *uptake of these toxins*, using animal and human models, should be assessed. Measurements of toxin exposure or biomarkers for disease risk must also be biologically relevant and must be associated with a disease state or risk for disease. The extent of tobacco toxin exposure must not solely rely on machine measurement, but must rely on human measurement that takes into account use patterns and amounts. These human measurements should also take into account differences in individual susceptibility to disease and biological differences, such as metabolism, that will determine the amount of tobacco toxins exposure. Prior studies with "light" and "mild" low yield cigarettes have shown that reduction of mortality and morbidity did not accompany the use of these lower tar and nicotine yield cigarettes because smokers compensated for the lower yield of nicotine by puffing longer, inhaling more deeply, or smoking more cigarettes (National Cancer Institute, 2001). The lesson learned from the lower yield cigarette story is that an accurate measure of tobacco toxin exposure is only determined by observing the amount of exposure among human cigarette smokers.

Third, the prevalence of use and population effect must be determined. Even if the toxin exposure is reduced on an individual level, the total amount of exposure and therefore harm on a population level may be increased. That is, because these products may be perceived as safer, individuals who may have never smoked may initiate smoking, smokers who are considering or will be considering cessation may continue to smoke or those who have quit may relapse. Again, using the lower yield cigarettes as an example, a significant number of smokers believed that these cigarettes were safer, which may have led to a number of smokers choosing to continue smoking, rather than quit (Stratton et al., 2001).

To date, the only proven methods to reduce the tobacco-related mortality and morbidity are prevention and cessation. No information is currently available indicating the amount of tobacco toxin reduction that is necessary in order to achieve a reduction in disease risk or whether the population interested in using these products would derive any beneficial effects given their long history of tobacco use or current disease state. Furthermore, no information is available on whether efforts at prevention and cessation would be compromised as a result of advertising products as reduced risk. Therefore, it is imperative that a system be in place not only to assess the harmful or beneficial effects of these products on an individual level, but also on a population level and that messages of cessation or prevention are not compromised.

Is it feasible to develop a combusted, cigarette-style product that is less harmful to the individual smoker and to the public at large?

The same issues that are discussed with the reduced exposure/reduced risk products pertain to the combusted, cigarette-style product.

Does smokeless tobacco represent an acceptable alternative to smoking cigarettes? Could it be considered a reduced-risk product?

The data is currently not sufficient or available to allow a yes response to this question. On a superficial level, the answer appears to be yes because use of the product does not involve combustion. However, when exploring the issue in more depth, many significant concerns are evident. Smokeless tobacco is not a harmless product. The use of smokeless tobacco results in addiction and smokeless tobacco use results in increased disease states (e.g., oral, throat and neck cancer, oral pathologies, increase in cardiovascular risk factors, and fetal toxicity). The extent of these harms to health is dependent on the toxins in the product as well as the duration and amount of use. The products in the United States vary in toxin levels (Hoffman et al., 1995). The most widely used smokeless tobacco product contains the greatest amount of toxins. Other products, typically those products that are not widely used, contain less amounts of toxins. It is important to note that even smokeless tobacco products with the lowest amounts of nitrosamines have levels that are thousands times greater than the permissible limits established for consumer products (USDHHS, 1986). Determining whether smokeless tobacco could be considered a reduced risk product involves looking at the impact of marketing this product as such on an individual as well as population level.

On an individual level, the amount of toxin exposure will depend on the amount and pattern of use. For example, the effect of dual use of smokeless tobacco and cigarettes is unknown. Potentially, dual tobacco users can achieve higher levels of exposure compared to those who use only one product (Wetter et al., 2002), leading to greater risk for disease. Additionally, little is known as to whether any beneficial effects can be experienced among cigarette smokers who have switched to smokeless tobacco, particularly after years of exposure to cigarettes. Minimal reduction in disease may be particularly true if the population of smokers who decide to use smokeless rather than quit are already a more physically compromised population of users. Therefore, it is important that these issues be examined prior to determining whether smokeless tobacco products confer reduced risk.

On a population level, the impact these products have on health will depend upon type and amount of marketing they receive. If tobacco companies are allowed to market their products as reduced risk, the ensuing public perception of these products and the impact resulting from these perceptions is unknown. We do not know if there would be a higher number of smokeless tobacco initiates, as observed in the United States between the 1970s and 1990s when significantly more advertisements for smokeless tobacco were evident. Furthermore, it is unknown whether ex-smokers, who are struggling to remain abstinent or to quit, would resort to smokeless tobacco products, rather than medications that have been proven to result in significantly less toxin exposure (Hatsukami et al., 2003). Finally, it is unknown whether individuals who decided to take up smokeless tobacco because of its relative safety, would not graduate to cigarette smoking, which in

some studies has been shown to occur (Tomar, 2002; Haddock et al., 2001). Interestingly, in the United States, few people have switched from cigarettes to smokeless tobacco. In this competitive market among tobacco companies, the most likely scenario would be an increase in initiation of smokeless tobacco use and no decrease in smoking, particularly if the marketing efforts continue to be aggressive and claims are unbridled.

What are the research challenges related to tobacco harm reduction?

A *strong research agenda* is necessary prior to recognizing or allowing claims for reduced risk products. The main research challenge is to insure a mechanism that will allow for testing of these products independent of the tobacco companies, whether by existing governmental agencies, a newly formulated one or by independent research scientists. These agencies or testing sites would be responsible for testing the toxicity of the products, examining the effects of exposure of these toxins using animal models and examining the absorption of these toxins in humans. In addition, independent organization(s) or scientists could also examine the effects of different marketing strategies on public perception and consider and test methods to minimize potential harm. An organization would also need to conduct post-marketing surveillance to determine prevalence and use patterns using strategies that are not unlike ones that are developed to monitor drugs that have potential abuse liability (e.g., Schuster et al., 2003).

The six areas that represent research challenges are the following and have been excerpted or more fully described elsewhere (Stratton et al., 2001; Hatsukami et al., 2002).

- Developing reliable and valid surrogate biomarkers that measure level of toxin exposure and disease risk or disease states. Currently, there are a limited number of biomarkers that are available that will allow researchers to begin to examine reduced exposure products, however more sophisticated and relevant biomarkers need to be developed. One of the challenges is that the use of modified tobacco products, a novel delivery system, or a combination of products can result in unique toxin mixtures that remain undetected by existing measures.
- Determining the extent of reduction that is necessary to experience any reduction in risk for disease. For example, it is unknown whether a 30% reduction in exposure to nitrosamines has any beneficial effect.
- Examining how characteristics of the product interact with tobacco use behavior to affect tobacco toxin exposure and disease risk.
- Examining how and what individual differences impact response to a product and disease susceptibility as a result of product use. For example, tobacco users may vary in their degree of dependence and this difference may determine the extent of tobacco toxin exposure. Tobacco users may have specific genetic polymorphisms that will make them more sensitive to the effects of particular carcinogens.
- Examining the impact of messages and marketing of reduced exposure products on consumer and healthcare provider attitudes, knowledge, perception, and beliefs. Finding ways and avenues to communicate information that will lead to the greatest net public health benefit.

- Developing a comprehensive surveillance system so that prevalence, pattern and consequence of use of these products and conventional tobacco products are determined across age groups, gender, race or ethnicity.

Conclusion

In summary, in order to protect public health and avoid public health disaster, the following steps must be taken: 1) Strong messages about tobacco prevention and cessation should continue to be made to the public. Priority should be given to efforts to develop, promote and provide effective methods for tobacco cessation; 2) A strong research agenda must be developed; 3) Scientists or organizations that are independent of the tobacco companies must test, assess and determine the impact of these products on individual and population levels. Most importantly, regulatory authority over these novel tobacco products or claims of reduced risk is essential in order to insure critical evaluation, accurate information of these reduced risk products, and to minimize harm to the individual and society. It is critical that companies are required to submit their products and claims to the Food and Drug Administration *before* the products and claims are in the marketplace.

Thank you for the opportunity to present this material to you.

References

Haddock, C., M. Weg, DeBon, M., Klesges, R. C., Talcott, G. W., Lando, H. and Peterson, A. (2001). "Evidence that smokeless tobacco use is a gateway for smoking initiation in young adult males." Preventive Medicine **32**(3): 262-267.

Hatsukami, D. K., LeSage, M., Hecht, S., Murphy, S., Lemmonds, C., Joseph, A. and Benowitz, N. (2003) "Tobacco exposure reduction." Symposium presentation at the Society for Research and Nicotine Annual Meeting, New Orleans, LA, February 19-22.

Hatsukami, D. K., Slade, J., Benowitz, N. L., Giovino, G. A., Gritz, E. R., Leischow, S. and Warner, K. E. (2002) "Reducing tobacco harm: research challenges and issues." Nicotine & Tobacco Research **4**(Supplement 2):S89-S101.

Hoffman, D., M. Djordjevic, Fan, J., Zang, E., Glynn, T. and Connolly, G. N. (1995). "Five leading US commercial brands of moist snuff in 1994: assessment of carcinogenic *N*-nitrosamines." Journal of the National Cancer Institute **87**: 1862-1869.

National Cancer Institute. "Risks associated with smoking cigarettes with low machine-measured yields of tar and nicotine." Smoking and Tobacco Control Monograph No 13. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute, NIH Pub. No. 02-5074, October 2001

Schuster, C. R., Johansen, C.-E., Vocci, F. and Hatsukami, D. K, Eds.. (2003). "Conference on abuse liability assessment of CNS drugs." Drug Alcohol Depend **70**(Supplement 3): S1-4.

Stratton, K., P. Shetty, Wallace, R. and Bondurant, S. Eds. (2001). Clearing the Smoke: Assessing the Science Base for Tobacco Harm Reduction. Institute of Medicine. Washington, DC, National Academy Press.

Tomar, S. (2002). "Snuff use and smoking in U.S. men. Implications for harm reduction." American Journal of Preventive Medicine **23**(3): 143-149.

U.S. Department of Health and Human Services. (1986) The health consequences of using smokeless tobacco. A report of the Advisory Committee to the Surgeon General. NIH Pub. No. 86-2874, Bethesda, MD, April 1986.

Wetter, D., J. McClure, deMoor, C., Cofta-Gunn, L., Cummings, S., Cinciripini, P. M. and Gritz, E. R. (2002). "Concomitant use of cigarettes and smokeless tobacco: prevalence, correlates, and predictors of tobacco cessation." Preventive Medicine **34**: 638-648.